Remarks

Applicant has carefully reviewed the Office Action in this application, and in response thereto has amended claim 1 to incorporate features of dependent claims 2 - 4, and has cancelled the remaining claims. Claim 1 is believed to clearly define over the references, and favorable reconsideration is requested.

The present invention is directed to a titration system utilizing feedback to alter not only the titrant delivery <u>rate</u>, but also to reverse the <u>direction</u> of the flow gradient. As now set out in the claims, this is accomplished by repetitively detecting characteristics of the mixed stream of titrant and sample, during an increasing gradient and during a decreasing gradient, to change the pump controller to thereby reverse the direction of the existing gradient. This reversal of the flow gradient (so that dF/dt, where F is the flow rate, will reverse its sign from positive to negative, or vice-versa) occurs each time a detector set point is crossed, and is produced by a feedback controller driving the variable pump which supplies the titrant.

The method of the invention achieves an economy of titrant volume and time that was not foreseen by the prior art. The present invention allows a titration to be carried out in three seconds while consuming 12 microliters of titrant, whereas the prior art represented, for example, by the cited reference to Nagy, uses a process which requires 10 times as much time and uses 200 - 400 times more titrant.

In the Office Action, the claims were rejected over Nagy (4,120,657) in view of Lopez Garcia and Becket (5,389,546).

The reference to Nagy does not suggest the present invention, but instead discloses a

fixed control program in which a reagent flow increases from zero to a preset maximum and then returns to zero (see column 5, lines 44 - 46). Although Nagy describes a "direct feedback" at column 5, lines 12 - 20, the purpose and operation of this feedback does not appear to be described in the patent, and therefore cannot be said to teach, or even suggest, applicant's invention, as admitted in the Office Action (page 3, last two lines).

The reference to Lopez-Garcia discloses a titration system having a variable pump driven by a function generator which produces a voltage ramp. As stated at page 73 second column, paragraph 4.2, the disclosed device operates along one flow gradient until it is completed (and the pump is delivering its maximum flow). Then it operates along a second gradient to decrease the pump to zero.

There is no disclosure of a feedback control in the Lopez-Garcia document, and, accordingly, no combination of these references can produce a feedback system of the type disclosed and claimed in the present application.

It is asserted in the Office Action that Lopez-Garcia shows that a flow reversal is essential, but it is respectfully pointed out that this reversal is not obtained through a feedback system, but through operating the pump starting at zero speed, reaching a maximum pump speed, and then returning to zero. This is not applicant's invention, and this disclosure cannot teach how to modify Nagy to obtain applicant's invention.

The Becket patent describes a system in which a feedback loop is used to maintain a titration at the precise equivalence point. However, that is not what applicant discloses or claims. Applicant's system differs from Becket for good reason: maintenance of a titration at its equivalence point is not a satisfactory solution to obtaining accurate determinations of an

Applicant's system differs from Becket for good reason: maintenance of a titration at its equivalence point is not a satisfactory solution to obtaining accurate determinations of an equivalence point, as explained in detail in the response to the first Office Action.

It is asserted that the feedback system of Becket could be used in Nagy or Lopez-Garcia, but even if this were to be done, the result would not be applicant's invention, as claimed.

Furthermore, the asserted combination would destroy both the Nagy system and the Lopez-Garcia system, changing both into systems that would be contrary to their own teachings, and preventing them from having either the structure of the function for which they were intended. Such a destruction of these devices is not an obvious combination of the teachings of these references, and is not taught by any of the references.

It is clear, therefore, that the combination of references asserted in the Office Action is not taught by the references themselves, is in fact contrary to their own teachings, and cannot be supported. Furthermore, even if the teachings of the references were to be combined, the result would not be a device that meets the terms of the claim now in this application, and accordingly that claim is clearly patentable.

The claim now presented combines the features of independent claim 1 and its dependent claims, and thus raises no new issues. The single claim clearly defines over the art, and is believed to be clearly allowable. Entry of the amendment and allowance of the application is, therefore, respectfully solicited.

If any issues remain unresolved, however, it is requested that the Examiner call the undersigned.

Respectfully submitted/

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Date: October 30, 2003

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